ATTORNEY DOCKET NO. 21127.0007U1
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	)	
	)	
Lee, et al.	)	Art Unit: 1615
	)	
Application No. 10/332,547	)	Examiner: Channavajjala, LS
	)	
Filing Date: September 30, 2003	)	Confirmation No. 5510
	)	
For: DERMAL APPLICATION SYSTEM FOR AMINOLEVULINIC ACID	)	

SUPPLEMENTAL DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

NEEDLE & ROSENBERG, P.C.
Customer Number 23859

Sir:

I, MECHTILD LOEBEL, hereby declare that:

1. I am an employee of photonamic GmbH & Co KG (further called "photonamic"), and hold a Ph.D. in Pharmacy from the University in Kiel, Germany. I have over 20 years experience in the field of pharmaceutical development, with an emphasis on patch development in the last 5 years. At photonamic, I am responsible for all aspects of pharmaceutical development and report directly to the CEO.

2. Photonamic is the assignee of the above-referenced application relating to dermal application system comprising crystalline aminolaevulinic acid (ALA). I coordinated the experiments discussed herein, which were performed by one of the world's leading producer of dermal therapeutic systems on photonamic's behalf.

3. I present in this declaration evidence indicating that dermal application systems comprising ALA crystals in the size range of tens to hundreds of microns have a significantly and surprisingly higher rate of ALA release compared to a dermal application system with dissolved ALA, such as the system described in WO 95/05813.

As shown in Exhibit A submitted with the prior Declaration, 515 $\mu g/cm^2$ ALA were released/ permeated from a silicon polymer patch comprising ALA crystals (90-160 μm) in the first hour, whereas only 9 $\mu g/cm^2$ ALA was released and had permeated through an artificial membrane when the dissolved ALA was used (see Figure 1 of Exhibit A). Likewise, about 1500 $\mu g/cm^2$ of ALA were released/ permeated from a polyacrylate patch comprising ALA crystals (20 to 200 μm in size) in the first hour, with 72.5 % of all ALA released in the first 30 min (see Figure 2A of Exhibit A). Moreover, as shown in Figure 1 of **Exhibit B** (attached hereto), about 1000 $\mu g/cm^2$ (57%) of ALA were released/ permeated from a polyisobutylen polymer patch comprising ALA crystals (90-160 μm) in the first hour. Therefore, the rate of ALA crystal release is dramatically higher than what is observed in prior art dermal application systems using dissolved ALA. Moreover, these results indicate that the unexpectedly higher ALA release rates are independent of the polymer matrix used.

4. I declare that all statements made herein of my own knowledge and belief are true and that all statements made on information and belief are believed to be true, and further, that the statements are made with the knowledge that willful false statements are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such

willful false statements may jeopardize the validity of the application or any patent issuing thereon.

5. I further declare that the demonstrated effect of significantly increasing the release rate by dispersing ALA crystals of the defined size in a dermal application systems such as a polyisobutylen patch, was not foreseeable on the basis of WO 95/05813 and/or US 5,856,566 .

Date: 16.09.2008

M. Loebel

MECHTILD LOEBEL

EXHIBIT B

Figure 1:

Release / permeation profile of ALA from a polyisobutylen polymer patch (Oppanol®) through an artificial membrane. Patches were prepared using ALA particles sized 90-160 µm suspended in the matrix. Within one hour 57 % of all ALA was released.